patient does not, as a rule, show external marks which would lead one to suspect an injury of the spleen. The diagnosis is made clinically. Occasionally an injury that is apparently trivial can cause such a hemorrhage. We recall one schoolboy who jumped on a street-car. While holding an exercise book with one edge in the fold of the left elbow and the other against the flank, he received a bump on the elbow as he swung onto the car. This was sufficient to rupture the spleen. Another case, a small girl, fell off a garage roof; she received bilateral Colles's fractures and a ruptured spleen. One must, therefore, constantly keep the possibility of a ruptured spleen well in mind. When in doubt, explore. The dangers incident to a simple exploratory operation, with negative findings, are far less than the danger of overlooking some lesion, the neglect of which may be fatal.

F. PAUL O'HARA, M. D. (Medico-Dental Building. San Diego).—This timely article on the very interesting subject is of an especial appeal to me, since, upon reviewing the cases of ruptured spleen in this district two years ago, I found that only one-third of the cases were diagnosed and operated upon prior to autopsy.

The difficulty of diagnosis is emphasized by the authors, and usually only a diagnosis of some ruptured viscus in the abdomen is possible. The initial shock in a ruptured spleen of any severity is out of proportion to the findings and should make one suspect the pathology. In cases that are observed longer than twenty-four hours following an injury, and in which the initial shock is overcome, the majority, if not all the cases, show a rather marked rise in blood pressure above normal, even in young people, which persists unless severe hemorrhage occurs, and lasts as long as several months following splenectomy. This interesting phenomena has not been satisfactorily explained by any investigators.

In some of the cases that I have seen, it is remarkable that the patient has gone back to his home for a period of a week or so following injury without a diagnosis being made, when the release of a blood-clot with resultant hemorrhage causes him to return with a typical picture. Another diagnostic point, which is not present, however, in all cases, is hematemesis of old blood, which possibly may occur due to the close association of the blood supply of the spleen and the stomach. The emphasis of close, continued reëxamination of these cases by the authors is to be commended, and the prompt, proper carrying out of splenectomy results in complete recovery in a surprising majority of cases. The use of autotransfusion is sometimes a life-saving procedure, but in all events transfusion or infusions should be saved until the hemorrhage is stopped by the performance of splenectomy.

IS PARESIS (DEMENTIA PARALYTICA) CURABLE?*

RESULTS IN PERSONALLY TREATED CASES

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DISCUSSION *by Samuel D. Ingham, M. D., Los Angeles; Benjamin W. Black, M. D., Oakland.*

THE clinical terms, general or progressive paresis of the insane, or dementia paralytica—paresis, in common parlance—given us by the older writers, describe only the final stages of this disorder, as seen in institutions and neglected cases. These terms are still applied to the earlier stages of the disease, when physical weakness or advanced mental disintegration is not evident. Our knowledge of paresis has outgrown the nomenclature, and there is need of a more descriptive term having a precise clinical and pathological foundation; however, the term is well established by usage and no descriptive terminology has satisfactorily replaced it. The disease is a pathological entity and is one of the few neuropathological conditions which may be microscopically diagnosed. To the classical description of Alzheimer [1] only a few additions have been contributed in recent years, notably the presence of the Spirochaeta in brain tissues and the characteristic iron deposits in the adventitia of the blood vessels. He had already (1904) expressed the opinion that rod cells, now classified as microglia, were of mesoblastic origin.

The usual paretic brain observed at necropsy shows a predilection of the pathologic process for the anterior parts of the brain, and thickened and adherent membranes over the shrunken cortex. Microscopically, both chronic inflammatory and degenerative cortical lesions are present. The relationship of these associated lesions has never been satisfactorily explained. Alzheimer has discussed mental symptoms in syphilitic brain lesions and classifies the nonparetic forms as vascular, gummatous, and meningiomyelitic (parenchymatous). In the latter form he particularly calls attention to the important association of the syphilitic meningitis with the essential brain changes. This writer discards the meningeal theory of paresis on the basis that in the early stages of the disease the superficial cortical lesions may be so slight and lesions in the deeper cortical layers so marked, that a causal relationship is not to be reasonably entertained. As these meningeal changes are not only hyperplastic, but also infiltrative, the reservation is made, however, that they may exert a determining influence on the manifestations of the disease.

The lack of pleocytosis in the cerebrospinal fluid, in cases where necropsy shows markedly thickened cerebral membranes, suggests that these membranes were primarily the seat of an active meningitis, and later have become sclerosed, when the active process has been arrested. If this hypothesis is valid, an appreciable pleocytosis is to be expected in the first stages of the disease, and not necessarily in the later stages. Such a condition is comparable to pathological processes observed in tabes.

A high fluid pleocytosis, associated with a paretic curve and strongly positive syphilitic serology, is frequently met with in patients with symptoms of emotionalism, nervousness, tremor, and heightened reflexes, who are often referred to a neuropsychiatrist with a Wassermann-fast blood. Symptomatology does not disturb the patient so much as consciousness of persisting syphilis. Indeed, it is quite probable that such cases, because of disregard of symptoms, often remain undiagnosed and untreated, until some definite mental or moral aberration enforces medical observation and care. Whether such early cases show a characteristic pathology of paresis is unknown, as only a chance necropsy could definitely decide this question.

If acute syphilitic meningitis affects the base of the brain, cranial nerves are involved; if it affects the cortex, lancinating headaches, tendency to somnolency, hypo-activity, and symptomatic complaints of the patient, differentiate this form from

* Read before the Neuropsychiatry Section of the California Medical Association at the sixty-sixth annual session, Del Monte, May 2–6, 1937.

paresis. The question then arises whether syphilis of the convexity may be a transient pathological state of paresis of essentially meningitic form, which, when progressive, determines paresis. Acute cases of this sort which come to the attention of the physician are generally recognized and treated, and it is further conceivable that beginning paresis may thus be aborted. Surely, paresis, comparable to the Argyll Robertson pupil, does not spring from the brain in its fully developed form, as did Minerva from the forehead of Zeus when his head was split with an axe to relieve a headache.

Pathological mutation in syphilitic brain processes, following therapy, is quite possible. It is now common knowledge that a paretic type of colloidal curve, indicating a high grade of parenchymatous involvement, may be broken down to a curve of cerebrospinal syphilis type. This will be strikingly demonstrated in the cases about to be reported.

IMPORTANCE OF PROPER THERAPY

It is not the purpose of this paper to enter into a discussion concerning the determination of paresis in an individual case, whether it is due to a particular strain of spirochaeta or to a constitutional tendency, but to emphasize that in early cases of brain syphilis which are clinically and serologically paresis, sustained and adequate therapy may effect a remarkable improvement, to the degree that the disease is arrested, and for all practical purposes, cured. This leads to a consideration of what is meant by the term "cure" in syphilis. Strictly speaking, an infectious disease process is cured only when the infective agent is definitely eliminated. This would postulate, therefore, negative tests for syphilis in symptomatically arrested patients observed over a considerable period of time. The term "cure" may be used properly, I believe, in cases which show no symptomatic effects, in so far as can be determined, even in the presence of serological signs of syphilis in attenuated form. Recovery is perhaps a better term. It may be this latter use of the term on which certain institutional statistics have been given us. I would particularly refer to a report on the treatment of dementia paralytica by the Mental Hospitals Committee of the London County Council [2] of 1936. It was pointed out in this report that before the advent of modern therapy there was no real recovery from the disease. In the six years from 1930-1935, inclusive, 1,914 cases were treated with modern methods. This series was compared with 2,545 cases in a six-year period, from 1908-1913, inclusive, when modern treatment was not in use. A comparison shows that in cases treated by modern methods the mortality rate had been halved, one-fifth of the cases had been discharged, the cure in the majority being permanent, and many of the persons discharged had filled positions of responsibility.

TREATMENT

It is questioned whether any fixed therapeutic regimen can be laid down for general application. The patient, as well as the disease, must be considered and studied. From the standpoint of the patient, maintenance of weight, general physical condition, and tolerance and response to given remedies must ever be borne in mind. Anemia, infections, and concurrent debilitating factors or habits must be combated and, if possible, removed. Alcohol should be proscribed or taken in extreme moderation. Exhaustion and fatigue are to be avoided. Whereas such general indications of therapy appear obvious, there is danger of neglecting the patient by treating the disease only, expressed by positive serology, and to base indications for treatment principally on the latter findings. Because of such considerations it has been our practice to administer interrupted, rather than continuous, treatment. It is desirable, however, to make a complete serological check after each course of treatment.

Malaria, in my experience, has proved the most efficient remedy in paresis, for there is fair evidence, according to the investigations of Breutsch [3] and others, that malaria exerts a favorable biological action in addition to the hyperpyrexia. In a number of my cases malarial therapy has been repeated; in one case the malaria was mistakenly believed to be terminated, and the patient carried the latent infection over a period of months. Hyperpyrexia, by hot baths, has been used in a few cases as a substitute for malarial treatment. Other means, as by typhoid vaccine, hot-air baths, and blanket packs, have been reported as giving satisfactory results.

Next to malaria in therapeutic efficiency, I place intraspinous therapy, and the modification of the Swift-Ellis treatment devised by the late Doctor Mehrtens, is used. Although less technical methods have largely replaced this form of therapy, it has a deserved and established place in the special armamentarium of treatment of this disease. Tryparsamid is a particularly valuable remedy in conjunction with malaria or fever therapy. In doses of one gram once or twice weekly, it is a comparatively safe remedy if ordinary precautions are taken in the initial doses to note either subjective or objective involvement of the optic nerve. It is not a remedy, however, that is applicable to each and every case; cases have been observed in which results have been disappointing in the failure of the patient to respond with the usual increase in appetite and weight and sense of well-being, and improvement of serology. Patients may even react unfavorably to this drug.

Heavy metal therapy is now chiefly represented by bismuth. I favor iodobismitol, which carries in combination iodin, a remedy formerly highly regarded in neurosyphilis, but undeservedly fallen in disuse. The same may be said of mercury; indeed, mercury, the iodids, and a sea trip, were the chief measures used in neurosyphilis before the advent of arsenical remedies, and not without benefit in a proportion of cases.

The arsphenamins are of value in cases where the meninges are permeable to these drugs, which permeability is in the neighborhood of 40 per cent. Their efficiency can be objectively determined by the serological response and the effect on a high fluid pleocytosis.

CASE 1.—*Chart of Treatment and Tests*

Treatment	Date	Tests								
		Leukocytes	Globulins	Colloidal Gold	Wassermann Fluid 1.0	0.5	0.3	0.1	Blood
Three years' general treatment immediately preceding observation	Aug. 18, 1923	10	Nonne + Noguchi +	5554433210	++++	++++	++++	++++	+++
August to October, 1923, ten intraspinous treatments; intramuscular mercury salicylate to tolerance	Oct. 26, 1923	6	Nonne + Noguchi +	5555554321	+++	+++	---	---	
November to December, 1923, eight tryparsamid injections, 1.5 to 3 grams	Dec. 4, 1923	3	Nonne + Noguchi +	4455431000	+++	+++	---	---	
December, 1923, to March, 1924, rest period									
March to May, 1924, eight tryparsamid injections; March to July, 1924, mercury salicylate; marked paranoid ideas	May 7, 1924	2	Nonne + Noguchi +	5555554321	+++	+++	---	---	
July to September, 1924, rest period	Sep. 11, 1924	2.5	Nonne tr. Noguchi tr.	5554321000	+++	+++	++-	±--	
September to December, 1924, ten intraspinous treatments; mercury salicylate	Dec. 5, 1924	7	Nonne tr. Noguchi tr.	3334421000	+++	++-	---	---	
December, 1924, to April, 1925, rest period; paranoid ideas in modified form	Apr. 23, 1925	1	Nonne + Noguchi +	5555553210	+++	+++	---	---	+++
April to August, 1925, nine tryparsamid injections; bismudol intramuscularly	Sep. 3, 1925	1	Nonne sl. tr. Noguchi sl. tr.	1223210000	+++	±--	---	---	---
August to December, 1925, rest period; mentally clear									
December, 1925, to January, 1926, eight tryparsamid injections	Jan. 14, 1926	1	Nonne + Noguchi +	3334542100	++-	---	---	---	---
January to December, 1926, rest period	May 14, 1926	—1	Nonne tr. Noguchi tr.	3233210000	+--	---	---	---	
December, 1926, to January, 1927, nine tryparsamid injections	Jan. 19, 1927	2	Nonne + Noguchi -	3333321000	---	---	---	---	
January to February, 1927, malaria; rest period	Jul. 12, 1927	2.5	Nonne tr. Noguchi tr.	2223211000	---	---	---	---	---
September to December, 1927, bismudol; December, 1927, to September, 1928, rest period	Aug. 18, 1928	—1	Nonne tr. Noguchi tr.	2222211000	---	---	---	---	---
September to November, 1928, sulpharsphenamin, bichlorid injections	Jun. 21, 1929	—1	Nonne tr. Noguchi -	1123221000	---	---	---	---	---
All treatment discontinued	Feb. 18, 1937	38	Heavy trace	Negative	---	---	---	---	---

In the serological control of medication a therapeutic response is considered favorable if a spinal fluid pleocytosis is reduced, the colloidal gold curve broken from paretic to middle-zone type, and the Wassermann reaction modified. If this serological improvement is effected with an associated improvement in the patient's mental and physical condition, we may confidently proceed in the majority of cases with the expectancy that the disease may be controlled and that a cure is possible. It is not contended that advanced cases with irreparable brain damage and atrophy, presenting marked dementia and debility, can ever be restored to normalcy by any treatment. However, even in such cases remarkable improvement may occasionally be observed.

REPORTS OF CASES

For obvious reasons, it is notoriously difficult to keep paretics under observation and treatment for any considerable period of time, except by an institutionally controlled regimen. Comparatively few extramural cases, therefore, have been followed a sufficient length of time to evaluate the final result of prolonged and intensive treatment. Frequently, after an initial satisfactory therapeutic response, these patients, with their characteristic optimism and lack of judgment, resist further treatment, and are, therefore, afterward inadequately treated or pass entirely from observation. Of those few cases in a considerable number, however, which have fulfilled the requirements of adequate, controlled therapy over a long period of time, four are here reported.

CASE 1.—Observation of thirteen years. A male rancher in the fourth decade was first observed in August, 1923, with symptoms of euphoria, impaired memory, mood changes, mental confusion, and paranoid ideas. His infection occurred ten years previously, following which he was inadequately treated. In the three years before consulting me, thirty to forty intravenous injections of arsphenamin had been administered; he was also given mercury. The physical and neurological examination was not remarkable, save for lack of pupillary light reaction and exaggerated tendon reflexes. His blood Wassermann was strongly positive. An analysis of the cerebrospinal fluid showed ten leukocytes per cubic millimeter, globulin increased, the

colloidal gold curve read 5554433210, the Wassermann reaction was positive in all dilutions. On hospitalization he was uncoöperative, demanded his release, and was only retained in the hospital by a ruse. Therapy was commenced by a series of ten weekly intraspinous treatments. After the fourth treatment some mental betterment was noted. Following this series of intraspinous treatments, the serology showed but little change, the colloidal curve remained paretic in type. During the period of intraspinous therapy he was also given intramuscular mercury salicylate to tolerance. In November, weekly injections of tryparsamid in one and a half to three-gram doses were commenced, and eight doses administered up to the end of 1923. In December, the first definite serological improvement was noted, the Wassermann reaction was negative in amounts of fluid less than 0.5 cubic centimeter, the colloidal gold curve was 4455431000. A mental rating at this time showed a mental age of 13.4 years, with obvious deterioration; comprehension of new situations was especially poor; the patient still showed paranoid tendencies and ideas of grandeur. He had spells of nervousness and excitability over small matters.

In the early part of 1924, after a rest period, he was given injections of leukocytic extract (Squibb), and from March to May eight injections of tryparsamid, one and a half grams each, and fourteen weekly intramuscular injections of mercury salicylate, one grain each, from March to July, when he developed a stomatitis. During this period considerable difficulty was experienced with the patient, who had left the hospital, because of paranoid ideas; threatening letters sent to former business associates were considered grounds for commitment by legal action, which, however, was deferred. These persecutory notions were such that the patient believed his life endangered, and would elaborate on experiences which showed marked ideas of reference in ordinary life situations. From September to December, 1924, he was given a second series of ten weekly intraspinous treatments, and with each treatment an intramuscular injection of mercury salicylate. The colloidal gold curve, which had remained paretic in type during the major part of this year, reverted in December to a middle-zone type, when the reading was 3334421000. In the beginning of 1925, paranoid ideas still persisted in modified degree; from April to August he was given intramuscular Bismudol [4] and nine tryparsamid injections; the colloidal gold curve again became paretic in type in April, but cerebrospinal in type in September, when the blood Wassermann first became negative and remained so permanently; he appeared mentally clear. In the early part of 1926 the Wassermann reaction in the fluid was only one plus in 1.0 cubic centimeter of fluid, and subsequent fluid Wassermanns were consistently negative. During this year the patient received but eight injections of tryparsamid in doses of one and a half grams. He had become mentally stabilized.

In the beginning of 1927, although the blood and fluid Wassermanns were completely negative, the colloidal gold curve read 3333321000. Five additional tryparsamid injections were given in January, after which he was given a course of malarial therapy. A recurrence of chills and fever followed temporary interruption of the disease by quinin. The malaria left the patient quite depressed and ill. In July his colloidal gold curve read 2223211000, and thereafter never reverted to the paretic type. From September to December, 1927, he was given bismuth injections. In the latter part of 1928 he received a course of intramuscular bichlorid and sulpharsphenamin, which latter remedy was poorly tolerated.

In June, 1929, the serology remained negative throughout; the colloidal gold curve read 1123221000. As the patient had made a mental and serological recovery, treatment was discontinued, his serology having been negative for approximately two years. He had successfully resumed occupation as a rancher, and has continued in a good state of physical and mental health up to the present. In February of this year, 1937, serological tests were repeated. The blood and fluid Wassermanns were negative, also the colloidal gold test. The globulins were reported, however, as a heavy trace, the leukocytes 38. In the light of the patient's lack of symptoms or complaints, and his occupational efficiency, I was inclined to regard these latter findings as a slip in laboratory technique. In any event, after an intensive, controlled therapy for five years, serological tests for syphilis have been negative for ten years, and no treatment has been given for eight years, during which last period there has been no recurrence of symptoms. In all, twenty-five cerebrospinal fluid examinations were made, which examinations were facilitated by the number of intraspinous injections. The tabulated list of these analyses showed a marked serological improvement following two years of intraspinous therapy and associated treatment by tryparsamid and mercury. The mental improvement fairly paralleled the serological improvement. Malaria was administered only after the disease had been controlled. This case well illustrates the interrupted type of treatment.

* * *

CASE 2.—Observation of eight years. A business man in the late twenties acquired his infection in 1918. He had been treated following his initial lesion, and also for six months prior to coming under my observation in October, 1928, by arsphenamin and heavy metals. The examination revealed tremor, marked stumbling over test phrases, left facial lagging, lively tendon reflexes, slowing of cerebration and poor digit memory. The clinical diagnosis was paresis, which was verified by serological tests: The blood Wassermann was strongly positive; cerebrospinal fluid Wassermann was also positive in all amounts of fluid tested; there were seven leukocytes per cubic millimeter, the colloidal gold curve read 4434342100. Following the lumbar puncture there was considerable mental excitement and confusion. Therapy was instituted by malarial inoculation; the malaria was interrupted on December 17, 1928, after the eighth paroxysm, because of shock and collapse; the fever registered 108 degrees Fahrenheit by rectum. Toward the end of January, 1929, after upbuilding by iron in the form of Blaud's pills, he showed a remarkable improvement; tremor, previously marked in both hands, ceased in the right hand, digit memory had improved, and he was emotionally stable. From February to May, 1929, he received thirteen intramuscular injections of one and one-half grains of bismudol. In June his colloidal gold curve reverted to a middle-zone type, the fluid Wassermann reaction was less strongly positive. Eight intraspinous treatments were given from June to October; at the conclusion of this series the colloidal test read 1122110000, the fluid Wassermann reading was essentially the same as in the previous test, the blood remained strongly positive. Directly following intraspinous therapy he was given a course of intramuscular sulpharsphenamin and bismuth to the end of the year. Following this intensive treatment, covering a period of somewhat over a year, he was given a rest period, then reinoculated with quartan malaria on May 15, 1930. The temperatures in a number of the paroxysms attained 105 [4] degrees Fahrenheit by mouth. In all, he had six paroxysms. In October, 1930, iodobismitol [5] was begun in 2 cubic centimeter intramuscular injections twice weekly; this was continued until the last of April, 1931; in all, forty-two such injections were given in the series. In August, 1931, the spinal fluid Wassermann was reported faintly positive, the colloidal gold curve was of the middle-zone type, not attaining a higher figure than 2. The blood remained positive. From August, 1931, to April, 1932, he received twenty-six injections of iodobismitol, two cubic centimeters each. At the conclusion of this series the patient was mentally stable and had resumed occupation. He did not report to the office for three years. In June, 1935, a cerebrospinal fluid test was negative throughout, the blood Wassermann gave an anticomplementary reaction. A further series of twenty injections of iodobismitol was administered. In September, 1936, the fluid was again entirely negative; the blood Wassermann anticomplementary, as before; titration revealed it suspiciously positive. He was then given eight injections of neoarsphenamin with instructions to report at future intervals for Wassermann tests. The last status showed no mental disturbance, no tremors, no emotional instability. At the present time he is successfully employed.

In this case the therapeutic attack was chiefly by means of malaria, and by bismuth in conjunction with iodin. From October, 1930, to April, 1932, he received a total of sixty-eight injections of iodobismitol in two cubic centimeter doses. There was a striking and persisting improvement after the first malarial inoculation. Comparatively little arsenical treatment was employed in this case. Tryparsamid was not given.

CASE 2.—*Chart of Treatment and Tests*

Treatment	Date	Leukocytes	Globulins	Colloidal Gold	Wassermann Fluid	Wassermann Blood
	Oct. 11, 1928	7	Nonne trace	4434342100	0.1 0.3 0.5 1.0 ++ ++++ ++++ ++++	++++
November, 1928, malarial inoculation February to May, 1929, bismuth injections						
	Jun. 20, 1929	4	Nonne neg. Noguchi neg.	2233321000	1.0 0.5 0.1 0.025 --- --+ +++ +++	
June to October, 1929, eight intraspinous injections	Oct. 22, 1929	9	Nonne neg. Noguchi neg.	1122110000	--- -++ +++ +++	+++
October to December, 1929, sulpharsphenamin, bismuth injections; rest period	Jan. 4, 1930					+++
May 15, 1930, malarial inoculation						
July to October, 1930, rest period	Jul. 22, 1930					+++ ++- +--
October to December, 1930, iodobismitol, 2 cubic centimeters twice weekly						
	Jan. 14, 1931	3	Nonne neg. Noguchi neg.	5444421000	--- --- -++ +++	+++
December, 1930, to May, 1931, iodobismitol May to August, 1931, rest period						
	Aug. 18, 1931	1	Nonne neg. Noguchi neg.	1222100000	--- --- --- -++	+++
August, 1931, to April, 1932, iodobismitol; mentally stable, at occupation						
	Jun. 14, 1935	2	Nonne neg. Noguchi neg.	1122110000	--- --- --- ---	Anticomplementary positive (?) on titration
June to October, 1935, iodobismitol						
	Sep. 19, 1936	2	Globulins trace	Negative	--- --- --- ---	Anticomplementary +++ on titration
September to November, 1936, neoarsphenamin, eight injections						

CASE 3.—Observation of nineteen years. A business man in the thirties was infected fourteen years previously and treated over a period of five years. The Wassermann reaction in the blood had been repeatedly negative prior to consultation with me in 1918, and but little specific therapy had been administered in recent years. He complained of neuritic-like pains in the legs. The neurological examination showed hyperactive reflexes, inversion of the right triceps reflex, and some disturbance of deep sensation in the left lower extremity. The clinical diagnosis was preataxic tabes. The Wassermann reaction in the blood at this time was positive. The cerebrospinal fluid Wassermann was also positive in 0.5 cubic centimeter of fluid and over; there were seventy-five leukocytes per cubic millimeter of fluid. The patient was not seen again until ten years later. In the interval he had been insufficiently treated, and no serological tests of the cerebrospinal fluid had been made. He complained at this time of extreme nervousness and tremor. The examination showed a suggestive Romberg, absent ankle jerks, fixed and myotic pupils, and tremor of the hands and tongue. No mental deterioration or psychotic symptoms were evident. The impression was an early form of taboparesis, which was confirmed by a serological recheck on the cerebrospinal fluid, which read: Leukocytes 45 per cent cubic millimeters of fluid, colloidal curve 5555431000, fluid Wassermann positive in amounts greater than 0.025 cubic centimeters. Six intraspinous treatments were given at intervals varying from one to two weeks. These were followed by severe constitutional reactions. Following the fifth treatment there was a slight apoplectiform seizure of the left extremities with increased reflexes on the affected side. After the intraspinous series the cerebrospinal fluid (May 29, 1928), showed a reduction of leukocytes to 24 per cubic millimeter of fluid, the colloidal gold curve read 3334321000, an indication of a break to a cerebrospinal type of curve. The fluid Wassermann remained unchanged. He was given thirty grains of potassium iodid daily. From June to November, 1928, sixteen weekly intravenous injections of one gram each of tryparsamid were administered, and during this period he was also given weekly intramuscular injections of bismudol, the dose varying from one and one-half to three grains each. A rest period was then prescribed until the latter part of March, 1929. In January, 1929, the cerebrospinal fluid tests showed marked improvement; there were but three leukocytes per cubic millimeter of fluid, globulins were within normal limits, the colloidal gold curve read 1121100000, and the fluid Wassermann reaction was positive only in amounts of fluid greater than 0.5 cubic centimeter. Clinical improvement was marked, tremor and nervousness were much less. From March to May, 1929, seven intramuscular injections of sulpharsphenamin of two-tenths gram each were given, then a rest period followed until November. From November, 1929, to February, 1930, three intraspinous treatments were given, and also sulpharsphenamin intramuscularly, following which the cerebrospinal fluid analysis remained unchanged. During the remainder of 1930 and 1931, heavy metal therapy, bismuth and mercury, was given, with frequent rest intervals; in all, but eighteen intramuscular injections were given in

this period. In March, 1932, there were no subjective complaints, tremor had disappeared, save for a slight coarse tremor of the protruded tongue. The reflexes, including pupillary reflexes, were unchanged, except for greater activity of the patellar reflexes. The cerebrospinal fluid serology remained practically the same, the blood Wassermann was slightly positive. From this time on intramuscular iodobismitol, in series of twenty injections two cubic centimeter doses each, twice weekly, has been given yearly to date. Each year a serological check has been made. The blood Wassermann became negative in 1933, and has remained so; likewise, the cerebrospinal fluid analysis this year (1937) was reported entirely negative for the first time. The patient is symptom-free of neurosyphilis, no further objective signs have developed, and he is occupationally fit. *In this patient it is significant to note that grave symptoms of central nervous system involvement developed during a ten-year period of insufficient treatment, during which time the initial pleocytosis of the fluid had receded.*

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CASE 4.—Observation of nine years. A lineman in the early thirties contracted his infection in 1920, following which he was treated for a period of eighteen months. In 1928 he entered a Veterans' Hospital because of a nervous breakdown, characterized by inefficiency in his work, lethargy, and forgetfulness. The records of the Veterans' Hospital state: He "received five injections of sulpharsphenamin and three of tryparsamid, also eight injections of mercury intramuscularly. On June 26, 1928, his blood Wassermann was positive, spinal fluid was positive, cells 21, gold curve 5555555431. He was inoculated with malaria on October 7, 1928, had fifteen paroxysms, maximum temperature 105 [6]. In view of the fact that he was taken out of the hospital against advice, we have no additional serological data."

The patient came under my care in November, 1928, at the request of his employers. The examination revealed a nervous-appearing man, with but little appreciation of the serious nature of his condition, and anxious to return to work. Vasomotor changes were marked in the extremities. Tendon reflexes were hyperactive, save for his ankle jerks. The left ankle jerk could not be definitely elicited. The general physical and neurological examination was otherwise quite negative, showing no abnormalities of pupils or the neuromuscular system. There were no tremors. A slight but characteristic euphoria was present, but no frank psychosis. The blood reaction at the time of this examination was strongly positive. He was given a course of eight weekly bismudol injections and kept under observation. In December, 1928, his cerebrospinal fluid serology was still strongly positive and of paretic type, but the cell count had dropped to three cells per cubic millimeter of fluid. From March to May, 1929, he was given weekly intramuscular injections of four-tenths gram of sulpharsphenamin; this was followed by eight weekly intramuscular injections of bichlorid of mercury, and a further course of eight sulpharsphenamin injections was given up to the end of 1929. During this year his condition, both physically and mentally, showed a distinct improvement. He had returned to ground work at his former occupation. In January, 1930, the blood Wassermann was reported negative, and thereafter remained so. The cerebrospinal fluid test showed two leukocytes per cubic millimeter, an increase in globulins, a persisting paretic type of curve, and a strongly positive Wassermann. A rest period until July, 1930, was followed by ten intravenous injections of tryparsamid and fourteen intramuscular injections of iodobismitol, two cubic centimeters each. In December, 1930, the cerebrospinal fluid showed no essential change. In 1931, a course of twelve sulpharsphenamin injections was given up to April; then followed a rest period of six months. Intramuscular injections of bismuth, alternating with iodobismitol, were resumed from September to December, nine injections in all. The cerebrospinal fluid analysis in December, 1931, still showed no appreciable change. Physically and mentally the patient appeared stable, tests of digit memory showed normal responses. At this period the question arose as to whether this patient might return to his original work as splicer, which necessitated working aloft. The company took the position that a man who had neurosyphilis could not ever be considered a good risk in a hazardous occupation. However, in view of this excellent occupational record and satisfactory response to treatment, he was permitted a trial, and has since been continuously working aloft as a splicer. From December, 1931, to July, 1932, there was a rest period. He was then given eight intravenous injections of silver salvarsan of two-tenths gram each. This was the only therapy administered during 1932. In January, 1933, the cerebrospinal fluid colloidal gold curve broke to a middle-zone type: 1123210000. The fluid Wassermann remained unchanged. During the year he was given two courses of iodobismitol of eight injections each. A cerebrospinal fluid test in June, 1934, showed the serological tests unchanged. During this year he received but eight injections of iodobismitol, commencing in June. In June, 1935, the Wassermann reaction in the fluid was positive only in 0.025 cubic centimeter of fluid; in this year he was given two courses of iodobismitol of eight injections each. In July, 1936, the cerebrospinal fluid showed a slight increase in the colloidal gold reaction, which still maintained a middle-zone curve; also a slight increase in the Wassermann reaction. In 1936, from July to October, he was given a course of twenty Bismarsen [6] injections of two-tenths gram each, intramuscularly. In April, 1937, the cerebrospinal fluid Wassermann was positive in 0.25 cubic centimeter of fluid, globulins two plus, there were three leukocytes per cubic millimeter, the colloidal gold curve read 0123210000. This patient is free of symptoms. He has remained continuously at work, with an excellent record of occupational performance. At his suggestion, improvements in tools used in his work have been adopted by his employers.

SUMMARY AND CONCLUSIONS

The present state of our knowledge regarding the nature and treatment of paresis is briefly reviewed. It is suggested that meningitis of the convexity is an important pathogenetic factor in the determination of this particular type of neurosyphilis.

Early stages of the disease are characterized by an appreciable pleocytosis and signs of meningoparenchymatous irritation, without evidence of any marked organic changes of essential brain tissue.

Detailed treatment of four cases—two well developed and two beginning paretics—is here reported, the duration of treatment and observation covering periods of thirteen, eight, nineteen, and nine years, respectively.

The typical fluid serology of paresis in three of these cases has been rendered negative by intensive treatment, and has remained so, with corresponding relief of symptoms for a sufficient length of time to justify the claim of a cure.

The remaining case, although not completely cleared serologically, has been transmuted to a benign cerebrospinal type.

All of these patients are symptom-free and occupationally active.

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4. Bismudol (Metz), Bismuthphenylformitate, 3 grains.

5. Iodobismitol (Squibb), Sodium Iodobismuthite Compound.

6. Bismarsen, D. R. L. (Abbott), Arsenic and Bismuth.

DISCUSSION

SAMUEL D. INGHAM, M. D. (727 West Seventh Street, Los Angeles).—The title of this paper suggests two possible answers corresponding to two different aspects of the question. If cure is considered to be a complete eradication of all the living organisms of syphilis from the body, we are not yet in a position to answer the question in the affirmative. If, on the other hand, we consider the question from the clinical aspect, we may be justified in stating that paresis can be cured symptomatically, even if it cannot be demonstrated that all the spirochaete of syphilis have been destroyed.

Accumulating statistics are impressive in demonstrating the fact that the modern treatment of paresis gives a higher percentage of better remissions than has ever been accomplished in the past. Of the modern methods of treatment, fever therapy is preëminent. There is still some difference of opinion in regard to the efficiency of artificial fever as compared with malaria, but I am inclined to favor the artificially induced hyperthermia for two main reasons: first, that the temperature reaction is entirely controllable at the will of the operator; second, the treatment is less exhausting to the patient and does not cause anemia—in fact, patients often gain in weight and improve physically during a course of treatments. There seems to be a definite correlation between the height of the temperature attained during the treatments and the success which follows. A series of treatments in which the temperatures are more than 106, or even 107 degrees Fahrenheit, are often necessary for best results.

Of the available drugs, bismuth has to a large extent superseded mercury. Tryparsamid is generally accepted to be the best form of arsenic. Alternate courses of intramuscular bismuth and intravenous tryparsamid are commonly used after a course of fever therapy as a matter of precaution even when the remission is already established.

The duration, as well as the character, of the remissions following modern treatment are better than the spontaneous remissions. The longest observation I have made is in the case of a patient who was given the malaria treatment twelve years ago, and has been working continuously in a responsible position and with a number of promotions in a large corporation over a period of twelve years. A recent patient treated in the acute stage received twelve fever treatments; maximum temperature, 108 degrees Fahrenheit; prompt remission; returned to work about two months after termination of treatments. The patient has continued to work with full efficiency and has received promotions since his recovery.

It seems to me that the best clinical evidence of curability of a disease like paresis is the promptness and the duration of recovery. Judged by this standard, early paresis is curable in a high percentage of cases.

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BENJAMIN W. BLACK, M. D. (Highland Hospital, Oakland).—The paper presented by Dr. Walter F. Schaller is a distinct contribution to the newer concepts of the dreaded disease, paresis. Having his own study of these cases in mind, Doctor Schaller stresses the term "paresis" to apply only to late manifestations, and properly makes the point that the entity under consideration does not spring from the brain in its fully developed form, with the observation of the new pathology in which the questions arise whether there is a transient pathological state of paresis, when essentially in the early form it presents the signs of meningococcic parenchymatous irritation. It is an interesting observation, particularly when it presents at this stage of the disease no marked organic changes of essential brain tissue. It is also of great interest, and stress should be placed on the statement that paresis at this stage may be aborted.

Many clinicians have long recognized the stage in the diagnosis; it seems not unusually difficult, but the important thing about the discussion would make clinicians conscious of the opportunities presented for beginning treatment which must be long continued.

Doctor Schaller has presented a series of cases showing in great detail his observation, diagnostic procedures, as well as treatment rendered over a period of as many as nineteen years. He has shown remarkable results, as all of the patients presented are symptom-free at this time and are occupationally active. An optimistic note in the treatment of this dreaded disease creeps through the discussion of these patients and their care. This, too, indicates much more than the paper would indicate: the painstaking attention given, the careful treatment provided, and the necessary arduous task of follow-up over this long period of time. Doctor Schaller has made a distinct contribution to the literature in the preparation of this paper; and to all who are concerned with the treatment of such cases as well as their early diagnosis, it should be a source of encouragement and at the same time it should point to a demand for early diagnosis and continued prolonged treatment. I am glad to have had the privilege of discussing this important paper.

THE TREATMENT OF TYPHOID FEVER IN CHILDREN, BY MEANS OF LYSED VACCINE

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DISCUSSION *by K. F. Meyer, Ph. D., San Francisco; Gregory Shwartzman, M. D., New York City; C. O. Mitchell, M. D., Fresno.*

TYPHOID fever is a disease of considerable mortality. In sixty-five cases admitted during the past ten years to the Fresno General Hospital there were eight deaths, a mortality rate of 12.3 per cent. Any measure which offers assistance in the treatment of this infection, therefore, merits consideration. Much attention is being given at present to biological therapy. The use of vaccine in typhoid began with Wright in 1898. In the preparation of Wright's vaccine, cultures of typhoid bacilli are killed by heat. It has recently been shown that the use of heat and chemicals as a devitalizing agent in the preparation of vaccines brings about denaturation with resultant loss of antigenic activity.[1] Vaccines in which this denaturation is reduced have been prepared by various methods.

TWORT-D'HERELLE STUDIES

In 1916-1917 Twort and D'Herelle introduced bacteriophage. Its chief use was in infections caused by bacillus of dysentery, staphylococcus and colon-group infections of the urinary tract.

There has been considerable discussion as to the nature of the lytic principle responsible for the Twort-D'Herelle phenomenon. It was at first thought that it was a living parasite of bacteria, alive and ultramicroscopic. Northrop and Krueger,[2] however, showed that it obeyed definite mathematical laws, and was in effect a chemical substance related to enzymes. The mechanism of bacteriophage activity is thought to be either through the propagation of bacteriophage in the blood stream, with resultant lysis of bacteria, or through the tissue response to the antigen released from the bacteria of lysis. Krueger, Lich, and Schulze[3] found no evidence of increase in the bacteriophage titer of the blood serum following the injection of bacteriophage. Moreover, the amount of bacteriophage present was wholly insufficient to induce bacterial lysis. Therefore, they concluded